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10/542,495	01/18/2006	Etienne-Emile Baulieu	03715.0148	7023

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FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
CHUI, MEI PING	
ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
05/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,495	BAULIEU ET AL.	
	Examiner	Art Unit	
	MEI-PING CHUI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *7,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *n/a*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Action

Receipt of Amendments/Remarks filed on 07/22/2008 is acknowledged. Claims 1-12 are pending in this application. Claims 1-6, 8-10 have been amended in the response filed on 07/22/2008.

Upon further consideration, Applicants' amendments necessitated the new grounds of rejection presented in this Office Action. Accordingly, this action is made **FINAL**.

Priority

Acknowledgment is made of Applicants' claim for foreign priority based on an application filed in France on 01/17/2003. However, it is noted that Applicants have not filed a certified copy of the English translation of the foreign application No. 03/00507 as required by 35 U.S.C. 119(b).

Status of Claims

Accordingly, claims **1-6, 8-10** are presented for examination on the merits for patentability as they read upon the elected subject matter and claims **7, 11-12** directed to non-elected inventions are withdrawn.

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Response to Arguments

Applicants' arguments filed on 07/22/2008, with respect to claims 1-6, 8-10, have been considered but are moot in view of the new ground(s) of rejection necessitated by Applicants' amendments.

New Grounds of Claim Rejection

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4-6 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in this rejection.

Claim 1 recites a treatment method "comprising the administration to a patient of an effective amount of a drug comprising 3β-methoxy-pregna-5-ene-20-one or a molecule derived from pregnenolone that contains a 3-methoxy function...", which is indefinite because the general accepted plain meaning of "a drug" is defined as **"a substance"** used as a medicament or in the preparation of medicament, or a substance intended for use as a component of a medicine (see Merriam-Webster Online Dictionary-Definition for Drug). It is unclear whether Applicants intend to claim the drug itself (contains only 3β-methoxy-pregna-5-ene-20-one or a molecule derived from pregnenolone that contains a 3-methoxy function) is administered to a patient or Applicants intend to claim the drug, which may also contain administration vehicle, i.e.

carrier, is administered to a patient. Therefore, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention, and thus rendering the claim indefinite.

Claims 2, 4 and 8 are also rejected because they depend from claim1, and thus incorporate its limitation.

Claim Rejection - 35 U.S.C. § 102

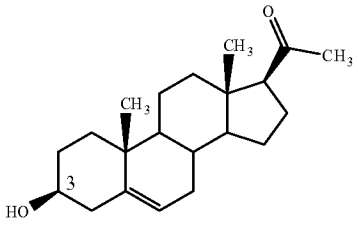
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102(b) that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

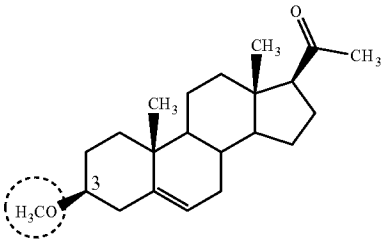
Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by The Merck Index (Twelfth Edition, 1996: page 1328, compound 7915), as evidenced by Chemical Book (retrieved via www.chemicalbook.com for the structure of pregnenolone methyl ether).

Instant claim 9 is directed to a drug consisting of 3-methoxy-pregnenolone (or refers as 3-methoxy-PREG in instant claim).

The Merck Index (1996) discloses the structure of the compound pregnenolone (page 1328: compound No. 7915 and see below) and discloses the physical property of its methyl ether derivative: pregnenolone methyl ether (page 1328: compound 7915, last two lines and see structure below):

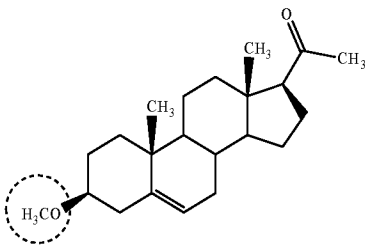


pregnenolone (parent compound)



pregnenolone methyl ether

Since the methylation of the parent compound pregnenolone can only occur at the C3-hydroxyl position to form the methyl ether derivative, the disclosure of methyl ether of pregnenolone will necessarily be the structure as set forth above (the structure at the right), as evidenced by Chemical Book (retrieved via www.chemicalbook.com), which discloses the structure of pregnenolone methyl ether (see Chemical Book printout and structure below):



pregnenolone methyl ether

Therefore, the disclosure of Merck Index anticipates instant claim 9.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

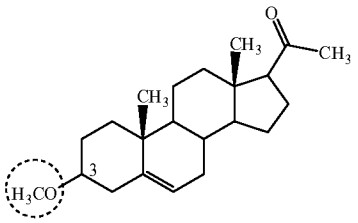
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

(1) Claims 1-6, 8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chopp et al. (U. S. Patent No. 6,245,757), as evidenced by Chemical Book (retrieved via www.chemicalbook.com for the structure of pregnenolone methyl ether).

Applicants Claim

Applicants claim a method of treating an acute or chronic lesion, or a degenerative disease of the nervous system, comprising the administration to a patient of a drug comprising 3β-methoxy-pregna-5-ene-20-one or a molecule derived from pregnenolone of the formula I (see below structure):



3-methoxy-pregnenolone

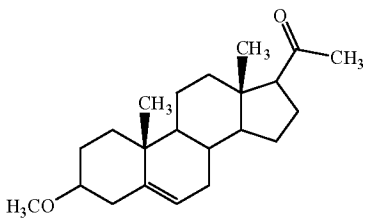
Determination of the scope and content of the prior art

(MPEP 2141.01)

Chopp et al. teach a method for the treatment of ischemic damage, i.e. damage due to stroke, comprising administering to a mammal afflicted with ischemic cell damage an effective amount of a pharmaceutical composition comprising progestin and a

pharmaceutically acceptable delivery vehicle (see Abstract and column 2, lines 28-45). Chopp et al. also teach that the method functions by the ability of the progestin to reduce the damage caused by ischemia, i.e. brain damage caused by cerebral ischemia, and the significant neurological functions improvement, as well as the enhancement of the ability of the brain to recognize after damage, be enhancing its intrinsic ability to compensate for injury (column 2, lines 38-45). As a result, the method provides whereby ischemic tissue, including tissue of the central nervous system or muscle tissue, can be treated so as to improve tissue survival and to hasten general bodily recovery (column 4, lines 22-26).

Chopp et al. then teach that the useful progestins for the treatment include pregnenolone methyl ether (column 5, lines 4-5 and structure below):



pregnenolone methyl ether

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Chopp et al. further teach that the progestin can be formulated as pharmaceutical formulations and administered to a mammal, i.e. human patient, in a variety of unit dosage forms, i.e. injection, adapted to the chosen route of administration, i.e. orally or parenterally includes intravenous route (column 5, lines 55-60 ad column 6, line 43). For oral administration, the progestin can combine with or more pharmaceutical excipients, so that the progestin is formulated to pass through the blood-brain barrier and enters the central nervous system at widespread sites and can effectively reduce infarct size following acute, focal ischemia, i.e. middle cerebral artery occlusion, when given before and after the onset of ischemia (column 6, lines 1-2; column 12, Example 2: lines 9-11; column 3, lines 63-67; column 4, line 1 and column 5, line 4).

In addition, Chopp et al. teach that each unit dosage form comprises the active progestin in amounts from 5-1000 mg (column 7, lines 14-17). Therefore, it meets the limitation for the claimed 3-methoxy-PREG is present in amounts "ranging from 50 to 2500 mg" as claimed in claim 8.

With respect to the recitation of the types of disease, i.e. an acute lesion, memory loss induced by a traumatic lesion, a cerebral lesion, ischemia, as claimed in claim 1 and claim 2, Chopp et al. teach that the treatment method utilizes the progestin for reducing ischemic damage due to stroke or myocardial infarction (see Abstract), wherein the treatable ischemia can be resulted from brain damage caused by cerebral ischemia (column 2, lines 38-41 and column 4, lines 9-12) or can be trauma resulting from ischemic insult (column 4, lines 13-20). It is also known that stroke is a type of acute ischemia and is commonly referred as brain ischemia or acute ischemic stroke. Therefore, the teaching of Chopp et al. meets the limitation of the recitation "an acute lesion" in claim 1 and the recitation "a traumatic lesion", "a cerebral lesion" and "ischemia", as claimed in claim 2.

With respect to the recitation of "wherein the drug also comprises an excipient that makes it possible to formulate...." in claim 3 is an optional claim language (see MPEP 2106 (II)). Further, Applicants broadly claim "an excipient" without any structural limitation. Therefore, the examiner takes the position that any excipient taught in the prior art reads on the recitation of claim 3 for the reason set forth above, since the prior art excipient and the claimed excipient are not structurally distinguish. In order to be limiting, the intended use must create a structural difference between the claimed

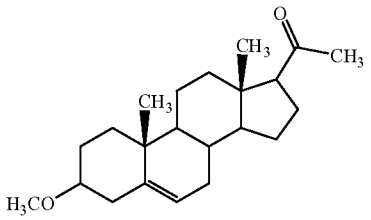
composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Chopp et al. teach a method of treating ischemic damage, i.e. damage due to stroke, comprising administering to a mammal an effective amount of a pharmaceutical composition comprising progestin, i.e. pregnenolone methyl ether, and a pharmaceutically acceptable delivery vehicle.

Chopp et al. do not particularly exemplify the use of pregnenolone methyl ether in the examples. However, Chopp et al. suggest that pregnenolone methyl ether can be used as one of the useful progestin for treating ischemic damage (see structure below and the pregnenolone methyl ether structure retrieved from Chemical Book via www.chemicalbook.com, as evidenced):



pregnenolone methyl ether

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Finding of prima facie obviousness Rational and Motivation

(MPEP 2142-2143)

It would have been obvious to a person of ordinary skilled in the art at the time the invention was made to follow the guidance of Chopp et al. to arrive at the instant invention.

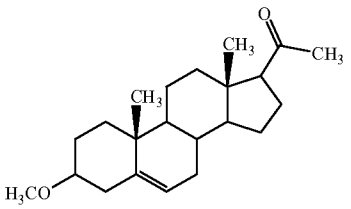
One of ordinary skill would have been motivated to do this because the prior art, namely Chopp et al., has already taught an effective method of treating ischemic damage, i.e. acute cerebral ischemia or brain ischemia, by administering to a human patient an effective amount of progestin in combination with an excipient. One of ordinary skill also would have been motivated to try the useful progestin, as suggested by Chopp et al., and then choose a desirable progestin and uses in the same method for treating ischemia, i.e. cerebral ischemia, as taught by Chopp et al.

From the teaching of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

(2) Claims 1-6, 8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stein et al. (U. S. Patent No. 2002/0072509), as evidenced by Chemical Book (retrieved via www.chemicalbook.com for the structure of pregnenolone methyl ether).

Applicants Claim

Applicants claim a method of treating an acute or chronic lesion, or a degenerative disease of the nervous system, comprising the administration to a patient of a drug comprising 3β-methoxy-pregna-5-ene-20-one or a molecule derived from pregnenolone of the formula I (see below structure):



3-methoxy-pregnenolone

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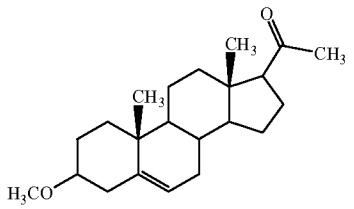
Determination of the scope and content of the prior art

(MPEP 2141.01)

Stein et al. teach a method and a composition for the treatment of neuro-degeneration following a traumatic injury to the central nervous system by reducing, or eliminating, neuronal cell death, edema, ischemia, and enhancing tissue viability, such that the treatment can enhance survival, proliferation, or/and neurite outgrowth of the neurons that either prevents or retards neuro-degeneration, i.e. a progressive loss of neurons in the central nervous system (page 2: [0016], lines 1-8). Stein et al. teach that the physiological events lead to the neuro-degeneration of the CNS tissues following a traumatic CNS injury, i.e. cerebral edema, increase in the immune and inflammatory response, demyelinization (page 2: [0017], lines 1-6).

Stein et al. also teach that the neuro-protective method is achieved by the administration of a therapeutically effective composition comprising a progestin, or a progestin metabolite, to a patient, i.e. human, wherein the useful progestin, i.e. pregnenolone methyl ether, can be used the method (page 2: [0018], lines 26-27 and 40, and the structure below), as evidenced by Chemical Book for the structure of pregnenolone methyl ether structure (retrieved via www.chemicalbook.com):



3-methoxy-pregnenolone

Stein et al. further teach that the composition may further comprise a pharmaceutically acceptable carrier vehicle, and the composition can be prepared into a pharmaceutically useful composition suitable for all forms of dose administration, i.e. injection and oral. Stein et al. teach that due to the traumatic CNS injury, the blood brain barrier may be more permeable for allowing the active compound to enter the cerebral spinal fluid (page 5: [0036-0037] and [0039-0041]).

With respect to the suitable amount of progestin in a dose, Stein et al. teach that such amount can be varied from about 1 μg to about 50 mg per kg of average body weight for the administration to a patient (which corresponds to about 14 mg to about 3500 mg per 70 kg of average body weight) (page 5: [0036-0037] and [0039-0041]).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Stein et al. teach a method utilizing a composition, which comprises an effective amount of progestin, i.e. pregnenolone methyl ether, and a pharmaceutically acceptable carrier vehicle for the treatment of neuro-degeneration following a traumatic injury to the central nervous system.

Stein et al. do not particularly exemplify the use of pregnenolone methyl ether in the examples. However, Stein et al. suggest that pregnenolone methyl ether can be used

as one of the useful progestin for protecting neuro-degeneration following a traumatic injury and enhance survival, proliferation, or/and neurite outgrowth of the neurons that either prevents or retards neuro-degeneration.

Finding of prima facie obviousness Rational and Motivation (MPEP 2142-2143)

It would have been obvious to a person of ordinary skilled in the art at the time the invention was made to follow the guidance of Stein et al. to arrive at the instant invention.

One of ordinary skill would have been motivated to do this because the prior art, namely Stein et al., has already taught an effective method of treating neuro-degeneration following a traumatic injury to the central nervous system by reducing, or eliminating, neuronal cell death, edema, ischemia, and enhances survival, proliferation, or/and neurite outgrowth of the neurons that either prevents or retards neuro-degeneration, i.e. a progressive loss of neurons in the central nervous system, by administering to a human patient an effective amount of progestin in combination with a pharmaceutically acceptable carrier vehicle. One of ordinary skill also would have been motivated to try the useful progestin, as suggested by Stein et al., and then choose a desirable progestin for use in the same method of preventing progressive loss of neurons in the central nervous system, as taught by Stein et al.

From the teaching of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in

the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new grounds of rejection presented in this Office Action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication from the Examiner should direct to Helen Mei-Ping Chui whose telephone number is 571-272-9078. The examiner can normally be reached on Monday-Thursday (7:30 am – 5:00 pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Johann Richter can be

reached on 571-272-0646. The fax phone number for the organization where the application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either PRIVATE PAIR or PUBLIC PAIR. Status information for unpublished applications is available through PRIVATE PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the PRIVATE PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/H. C./

Examiner, Art Unit 1616

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616